Claims

1. A protein variant which substitutes valine for phenylalanine residue in a binding domain of a protein having a biological response-modifying function by binding to a receptor, ligand or substrate.

2. The protein variant according to claim 1, wherein the protein is a cytokine.

3. The protein variant according to claim 2, wherein the cytokine is a 4-alpha helix bundle cytokine.

4. The protein variant according to claim 3, wherein the 4-alpha helix bundle cytokine is selected from the group consisting of CNTF, EPO, Flt3L, G-CSF, GM-CSF, GH, IL-2, IL-3, IL-4, IL-5, IL-6, IL-12p35, LPT, LIF, M-CSF, OSM, PL, SCF, TPO, IFN-α2A, IFN-α2B, IFN-β, IFN-γ, IFN-ω and IFN-τ.

5. The protein variant according to claim 4, wherein the CNTF, EPO, Flt3L, G-CSF, GM-CSF, GH, IL-2, IL-3, IL-4, IL-5, IL-6, IL-12p35, LPT, LIF, M-CSF, OSM, PL, SCF and TPO are altered by substituting valine for phenylalanine residue of amino acid residues between positions 110 and 180.

6. The protein variant according to claim 4, wherein the IFN-α2A, IFN-α2B, IFN-β, IFN-γ, IFN-ω and IFN-τ are altered by substituting valine for phenylalanine residue of amino acid residues between positions 1 and 50.

7. The protein variant according to claim 4, wherein the CNTF is altered by substituting valine for phenylalanine residue at a position 3, 83, 98, 105, 119, 152 or 178 of an amino acid sequence designated as SEQ ID NO.: 1.

8. The protein variant according to claim 4, wherein the EPO is altered by substituting valine for phenylalanine residue at a position 48, 138, 142 or 148 of an amino acid sequence designated as SEQ ID NO.: 2.

9. The protein variant according to claim 4, wherein the Flt3L is altered by substituting valine for phenylalanine residue at a position 6, 15, 81, 87, 96 or 124 of an amino acid sequence designated as SEQ ID NO.: 3.

10. The protein variant according to claim 4, wherein the G-CSF is altered by substituting valine for phenylalanine residue at a position 13, 83, 113, 140, 144 or 160 of an amino acid sequence designated as SEQ ID NO.: 4.

11. The protein variant according to claim 4, wherein the GM-CSF is altered by substituting valine for phenylalanine residue at a position 47, 103, 106, 113 or 119 of an amino acid sequence designated as SEQ ID NO.: 5.

12. The protein variant according to claim 4, wherein the GH is altered by substituting valine for phenylalanine residue at a position 1, 10, 25, 31, 44, 54, 92, 97, 139, 146, 166, 176 or 191 of an amino acid sequence designated as SEQ ID NO.: 6.

13. The protein variant according to claim 4, wherein the IL-2 is altered by substituting valine for phenylalanine residue at a position 42, 44, 78, 103, 117 or 124 of an amino acid sequence designated as SEQ ID NO.: 13.

14. The protein variant according to claim 4, wherein the IL-3 is altered by substituting valine for phenylalanine residue at a position 37, 61, 107, 113 or 133 of an amino acid sequence designated as SEQ ID NO.: 14.

15. The protein variant according to claim 4, wherein the IL-4 is altered by substituting valine for phenylalanine residue at a position 33, 45, 55, 73, 82 or 112 of an amino acid sequence designated as SEQ ID NO.: 15.

16. The protein variant according to claim 4, wherein the IL-5 is altered by substituting valine for phenylalanine residue at a position 49, 69, 96 or 103 of an amino acid sequence designated as SEQ ID NO.: 16.

17. The protein variant according to claim 4, wherein the IL-6 is altered by substituting valine for phenylalanine residue at a position 73, 77, 93, 104, 124, 169 or 172 of an amino acid sequence designated as SEQ ID NO.: 17.

18. The protein variant according to claim 4, wherein the IL-12p35 is altered by substituting valine for phenylalanine residue at a position 13, 39, 82, 96, 116, 132, 150, 166 or 180 of an amino acid sequence designated as SEQ ID NO.: 18.

19. The protein variant according to claim 4, wherein the LPT is altered by substituting valine for phenylalanine residue at a position 41 or 92 of an amino acid sequence designated as SEQ ID NO.: 19.

20. The protein variant according to claim 4, wherein the LIF is altered by substituting valine for phenylalanine residue at a position 41, 52, 67, 70, 156 or 180 of an amino acid sequence designated as SEQ ID NO.: 20.

21. The protein variant according to claim 4, wherein the M-CSF is altered by substituting valine for phenylalanine residue at a position 35, 37, 54, 67, 91, 106, 121, 135, 143, 229, 255, 311, 439, 446 or 485 of an amino acid sequence designated as SEQ ID NO.: 21.

22. The protein variant according to claim 4, wherein the OSM is altered by substituting valine for phenylalanine residue at a position 56, 70, 160, 169, 176 or 184 of an amino acid sequence designated as SEQ ID NO.: 22.

23. The protein variant according to claim 4, wherein the PL is altered by substituting valine for phenylalanine residue at a position 10, 31, 44, 52, 54, 92, 97, 146, 166, 176 or 191 of an amino acid sequence designated as SEQ ID NO.: 23.

24. The protein variant according to claim 4, wherein the SCF is altered by substituting valine for phenylalanine residue at a position 63, 102, 110, 115, 116, 119, 126, 129, 158, 199, 205, 207 or 245 of an amino acid sequence designated as SEQ ID NO.: 24.

25. The protein variant according to claim 4, wherein the TPO is altered by substituting valine for phenylalanine residue at a position 46, 128, 131, 141, 186, 204, 240 or 286 of an amino acid sequence designated as SEQ ID NO.: 25.

26. The protein variant according to claim 4, wherein the IFN-α2A is altered by substituting valine for phenylalanine residue at a position 27, 36, 38, 43, 47, 64, 67, 84, 123 or 151 of an amino acid sequence designated as SEQ ID NO.: 7.

27. The protein variant according to claim 4, wherein the IFN-α2B is altered by substituting valine for phenylalanine residue at a position 27, 36, 38, 43, 47, 64, 67, 84, 123 or 151 of an amino acid sequence designated as SEQ ID NO.: 8.

28. The protein variant according to claim 4, wherein the IFN-β is altered by substituting valine for phenylalanine residue at a position 8, 38, 50, 67, 70, 111 or 154 of an amino acid sequence designated as SEQ ID NO.: 9.

29. The protein variant according to claim 4, wherein the IFN-γ is altered by substituting valine for phenylalanine residue at a position 18, 32, 55, 57, 60, 63, 84, 85, 95 or 139 of an amino acid sequence designated as SEQ ID NO.: 10.

30. The protein variant according to claim 4, wherein the IFN-ω is altered by substituting valine for phenylalanine residue at a position 27, 36, 38, 65, 68, 124 or 153 of an amino acid sequence designated as SEQ ID NO.: 11.

31. The protein variant according to claim 4, wherein the IFN-τ is altered by substituting valine for phenylalanine residue at a position 8, 39, 68, 71, 88, 127, 156, 157, 159 or 183 of an amino acid sequence designated as SEQ ID NO.: 12.

32. A DNA encoding the protein variant according to any one of claims 1 to 31.

33. A recombinant expression vector to which the DNA according to claim 32 is operably linked.

34. The recombinant expression vector according to claim 33, wherein the recombinant expression vector has an accession number KCCM-10500, KCCM-10501 or KCCM-10571.

35. A host cell transformed or transfected with the recombinant expression vector according to claim 33 or 34.

36. A method of preparing a protein variant, comprising cultivating the host cell according to claim 35 and isolating the protein variant from a resulting culture.

37. A pharmaceutical composition comprising the protein variant according to any one of claims 1 to 31 and a pharmaceutically acceptable carrier.